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Summary of HBD East 2008 Think Tank Meeting

HBD East 2008 Planning Committee

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"Harmonization by Doing" (HBD) is an international activity for discussing and overcoming regulatory obstacles that may occur in promoting medical device clinical trials and approval review in parallel in Japan and the United States, based on actual practice ("Doing"). This activity is supported by cooperative efforts between the regulators, academic community, and medical device industry both in Japan and the U.S. Participants from Japan include the Ministry of Health, Labour and Welfare (MHLW), the Pharmaceuticals and Medical Devices Agency (PMDA), universities and medical institutions, The Japan Federation of Medical Devices Associations (JFMDA), and from the U.S., Food and Drug Administration (FDA), Duke University, and AdvaMed.

The HBD initiative was launched following an approach from activities initiated by the academic community in 2003. Trial symposiums were held and the first HBD West Think Tank meeting was finally held in January 2007. At this meeting, the principles, organization, and future prospects of HBD were discussed, and it was decided that activities will mainly focus on problems related to cardiovascular medical devices for cardiovascular in the foreseeable future.

HBD consists of a Steering Committee (SC) and four Working Groups (WGs) to carry out activities as follows.

- SC: Discussion of the policies of the entire HBD and each WG, and management of HBD activities
- WG1: Global cardiovascular device trials, consideration of a single protocol
- WG2: Postmarket registries
- WG3: Clinical trials infrastructure
- WG4: Regulatory convergence and communication

After the first HBD West Think Tank meeting, HBD activities have continued, such as a monthly SC conference calls every month, and closed meetings by each WG. On July 22nd and 23rd 2008, the second Think Tank meeting "HBD East 2008 Think Tank meeting" was held in the National Youth Center in Yoyogi, Tokyo. Professor Ryoza Nagai, Graduate School of Medicine, The University of Tokyo took up his post as the project supervisor of the Think Tank meeting. The planning committee, facilities committee, and funding committee consisting of the regulators, academic community, and medical device industry in Japan as well as the program committee consisting of the regulators, academic community, and medical device industry in both Japan and the U.S. were organized to manage the meeting. Participants in this meeting are as follows.

Japan	Regulators: 22	Academic community: 31	Medical device industry: 121	Subtotal: 174
U.S. ^(*)	Regulators: 5	Academic community: 4	Medical device industry: 18	Subtotal: 27
Total	Regulators: 27	Academic community: 35	Medical device industry: 139	<u>Total: 201</u>

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(* Including participants from Europe

Over the two days, each participating party spoke on the value of HBD and overview of HBD activities, as well as the Proof of Concept (POC) approach, and the WGs reported their progress. At the end of the meeting, a summary discussion was delivered. The major points in each session are as follows.

1) Overview of HBD

- FDA promised to be actively involved in HBD. In addition, “the Regulatory Roadmap” was presented by regulators in both countries.
- In GHTF, regulatory frameworks have been discussed. In contrast implementation ("Doing") and harmonization of the regulatory process. While, it is important for HBD to implement ("Doing") something in regulatory process, which leads to the identification of issues to be addressed and process improvement. It is also important to acquire experience and achieve good results through "Doing".

2) POC approach

- The ultimate aim of the POC approach is to accomplish the goals set by the WGs, identify issues to be addressed, and seek solutions in order to promote harmonization between Japan and the U.S.
- Collaborators for POC are necessary. They are recruited by active information disclosure of HBD activities.

The draft for discussion on recruitment method and selection process was presented by the regulators in both Japan and the U.S. and further discussion will be continued.

- It should be noted that participation in a POC project does not mean that the subject products of collaborators are handled in priority review process.

3) WG1 (Global Cardiovascular Device Trials)

- The activity policy aim is to implement aid in development and implementation of efficient clinical trials efficiently using a single protocol common to both to Japan and the U.S.
- The process by which a single protocol is generated is the key to success.

It is important to utilize the consultations (pre-IDE, early consultation) with regulators both in Japan and the U.S. from the early stages of development, and a cooperative approach with the regulators (through utilization of POC provided by HBD) is preferable.

4) WG2 (Postmarket registries)

- In the U.S., INTERMACS database system for post-marketing registry is functioning well.
- Development of a Japanese registry system is being considered, mainly by the Office of Safety, PMDA, so that good high-quality data equivalent to that obtained in clinical trials can be shared for proper evaluation of a device.

5) WG3 (Clinical trials infrastructure)

- Listing the candidate physicians/hospitals for selecting trial sites is a priority issue for the improvement in clinical trials infrastructure.
- It is important to improve clinical trials infrastructure while, taking the differences between medical devices and pharmaceuticals into consideration.

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6) WG4 (Regulatory convergence and communication between the regulator and business as well as government-to-government)

- There are no fundamental differences in good clinical practices (GCP) s between Japan and the U.S.

Case studies will be performed to develop practical solutions and provide /guidance for nonessential differences.

- Although there are no significant differences in items/sections between 510(k) STED (Summary Technical Documentation) and Japanese STED for third-party certification, it was found that there are differences in the specific contents of the items. Future Assessment/comparison will be performed based on products which need Minister's marketing approval in Japan /PMA products in the US. STED POC Assessments will be performed for harmonization of STED submission content and format. Careful examination is required to develop commonly-accepted STED

7) Summary

- Regulatory Roadmap presented by Japan and U.S. regulators isare an significant achievement of this meeting.
- To promote and expand transparency of HBD, it is necessary to disclose information through academic meetings, journals, and websites, and actively provide physicians with information.
- The way that the Regulatory Roadmap is implemented will be presented by the regulators in both Japan and the U.S.

At the end of the Think Tank meeting, regulators, academic community, and medical device industry in both Japan and the U.S. presented their views and expectations. The meeting concluded with the presentation of an overview for promoting HBD activities for the next year based on the achievements of this meeting.

Next year, the HBD West Think Tank meeting will be held in the U.S. It is important to keep goingkeep HBD activities going through SC conference calls, etc. As comments from participants indicated, it is crucial to promote HBD activities while keeping in mind that we need to provide patients with medical devices thatwhich areis demanded more quickly.